with a 25-year history of anticonvulsant drug-resistant complex partial seizures. Computer analysis of captured images revealed over 100 differentially regulated genes, some involved in neurotransmitter release, plasticity and signalling mechanisms. Other candidate genes were novel. Secondary validation with selected candidate clones re-gridded was undertaken by hybridizing newly constructed probes derived from further RNA samples from the same epileptic patient and control. This technology is an effective approach to analysing gene expression changes and may yield new targets from therapeutic intervention in epilepsy.

Association study of idiopathic primary generalized epilepsy (IGE)

A. Makoff*†, B. Chioza*‡, N. Curran†, P. Asherson‡ & L. Nashef§¶

*Department of Psychological Medicine, Institute of Psychiatry, London, UK; †Department of Neuroscience, Institute of Psychiatry, London, UK; ‡Social Genetic & Developmental Psychiatry Research Centre, Institute of Psychiatry, London, UK; §Kent and Canterbury Hospital, Canterbury ¶Kings College Hospital, London, UK

Twin studies have demonstrated concordance rates of up to 95% for idiopathic generalized epilepsy (IGE) in monozygotic twin pairs. There are a few rare mendelian forms of IGE, but most show a complex pattern of inheritance. The relative risk for IGE among first-degree relatives is in the range 5–10 suggesting that association studies will be required to detect the expected small gene effects. We have collected an initial sample of 100 probands with IGE and 100 ethnically matched controls. Our initial studies have focused on the metabotropic glutamate receptor type 7 (mGluR7) and the α4 nicotinic acetylcholine receptor subunit (nAchRα4). Mouse knockouts of mGluR7 result in an epileptic phenotype. Studies of a biallelic polymorphisms in mGluR7 are in progress.

Mutations within nAchRα4 have been shown to cause the rare dendelian epilepsy autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). An association study with a mixture of different IGE syndromes provides some evidence for association to nAchrα4. The gene for nAchRα4 lies only 50 Kb from a voltage-sensitive potassium channel gene (KCNQ2) in which mutations cause one type of another mendelian epilepsy, benign familial neonatal convulsions (BFNC). We are currently utilizing polymorphisms in the nAchRα4 gene and KCNQ2 in our sample.

Functional and structural findings in epilepsy demonstrated with diffusion weighted imaging

U.C. Wieshamnn, M.R. Symms & S.D. Shorvon

Epilepsy Research Group, Institute of Neurology, Queen Square, London, UK

Diffusion weighted imaging (DWI) is a magnetic resonance imaging technique which is sensitive to molecular motion of water. Transient or permanent changes of the microstructural organization of tissue, for example, widening or shrinkage of the extracellular space cause diffusion changes which can be detected by DWI. We used DWI to investigate patients with epilepsy. In a patient with focal status we detected transient diffusion changes which were likely to reflect neuronal dysfunction. During the interictal stage we found an increased diffusion in structural lesions associated with epilepsy. These included hippocampal sclerosis, tumours and most forms of brain damage. These changes were associated with a reduced anisotropy of water diffusion which is likely to reflect a breakdown of the structural organization. A reduction of anisotropy was the predominant finding in cortical dysgenesis.

In conclusion, DWI can show changes of water diffusion in focal status epilepticus. In addition, DWI provides information about the microstructure in lesions which may help to understand the pathophysiology of seizures.